AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for *in vivo* down-regulation of osteoprotegerin ligand (OPGL) activity in a mammal, the method comprising effecting presentation to the mammal's immune system of an immunogenically effective amount of a modified OPGL polypeptide having general formula I:

$$(MOD_1)_{s1}(OPGL_{e1})_{n1}(MOD_2)_{s2}(OPGL_{e2})_{n2}....(MOD_x)_{sx}(OPGL_{ex})_{nx} \quad (I)$$

-where $OPGL_{e1}$-$OPGL_{ex}$ are x B-cell epitope containing subsequences of OPGL which independently are identical or non-identical and which optionally contain foreign side groups in the form of at least one foreign T helper lymphocyte epitope, x is an integer ≥ 3, n1-nx are x integers ≥ 0 of which at least one is≥ 1, MOD_1-MOD_x are x modifications in the form of at least one foreign T helper lymphocyte epitope, MOD_2-MOD_X are modifications that are introduced between ~~the~~ preserved B-cell epitopes, and s_1-s_x are x integers ≥ 0 of which at least one is ≥ 1 if no optional side groups are introduced in the $OPGL_e$ sequences, whereby the ~~animal's~~mammal's own OPGL is down-regulated due to binding thereof to antibodies induced by immunization with the modified OPGL polypeptide,
OPGL being a protein which acts as an osteoclast differentiation factor and which has an amino acid sequence as set forth in SEQ ID NO: 2 for human OPGL.

2. - 4. (Cancelled)

5. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide includes an amino acid substitution in or deletion in or insertion in or addition to the OPGL polypeptide sequence, or any combination thereof.

6. – 7. (Cancelled)

8. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide includes a duplication of at least one OPGL B-cell epitope.

9. (Previously Presented) The method according to claim 1, wherein the foreign T-cell epitope is immunodominant in the mammal.

10. (Previously Presented) The method according to claim 9, wherein the foreign T-cell epitope is capable of binding to a large proportion of MHC Class II molecules.

11. (Previously Presented) The method according to claim 10, wherein the at least one foreign T-cell epitope is selected from the group consisting of a natural T-cell epitope and an artificial MHC-II binding peptide sequence.

12. (Previously Presented) The method according to claim 11, wherein the natural T-cell epitope is selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a *P. falciparum* CS epitope.

13. – 16. (Cancelled)

17. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide contains a modification in any one of positions 171-193, any one of positions 199-219, any one of positions 222-247, any one of positions 257-262, or in any one of positions 286-317, the amino acid numbering conforming with that of SEQ ID NO: 2.

18. (Original) The method according to claim 17, wherein the modification comprises a substitution of at least one amino acid sequence within a position defined in claim 17 with an amino acid sequence of equal or different length which contains a foreign T_H epitope.

19. (Previously Presented) The method according to claim 18, wherein the amino acid sequence containing the foreign T_H epitope substitutes amino acids 257-262 and/or 289-303 and/or 222-243 in SEQ ID NO: 2 or in a polypeptide where a cysteine corresponding to Cys-221 of SEQ ID NO: 2 has been substituted with Ser.

20. (Previously Presented) The method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of the modified OPGL polypeptide covalently of non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

21. (Previously Presented) The method according to claim 1, wherein the modified OPGL polypeptide has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

22. (Previously Presented) The method according to claim 1, wherein an effective amount of the modified OPGL polypeptide is administered to the mammal via a route selected from the group consisting of parenteral route; the peritoneal route; the oral route; the buccal route; the sublinqual route; the epidural route; the spinal route; the anal route; and the intracranial route.

23. (Previously Presented) The method according to claim 22, wherein the effective amount is between 0.5 μg and 2,000 μg of the modified OPGL polypeptide.

24. (Previously Presented) The method according to claim 22, wherein the modified OPGL polypeptide is contained in a virtual lymph node (VLN) device.

25. – 27. (Cancelled)

28. (Previously Presented) The method according to claim 22, which includes at least one administration/introduction per year.

29. – 56. (Cancelled)

57. (Previously Presented) The method according to claim 1, wherein the mammal is a human being.

58. (Previously Presented) The method according to claim 12, wherein the Tetanus toxoid epitope is a P2 or P30 epitope.

59. (Previously Presented) The method according to claim 22, wherein the parental route is selected from the group consisting of the intracutaneous, the subcutaneous, and the intramuscular routes.

60. (Previously Presented) The method according to claim 28, wherein the modified OPGL polypeptide is administered/introduced at least 2, at least 3, at least 4, at least 6 or at least 12 times per year.

61. (Previously Presented) A method for *in vivo* down-regulation of osteoprotegerin ligand (OPGL) activity in a mammal, the method comprising effecting presentation to the mammal's immune system of an immunologically effective amount of at least one modified mammalian OPGL polypeptide or analogue thereof,

wherein said modified mammalian OPGL polypeptide or analogue thereof comprises at least residues 158 to 316 of OPGL and is modified by the introduction of immunogenic amino acid sequences which are introduced such that inherent B-cell epitopes in said OPGL polypeptide or analogue are preserved; whereby immunization of the mammal with the modified mammalian OPGL polypeptide or analogue thereof induces production of antibodies against the mammal's own OPGL polypeptide which down-regulates the mammal's own OPGL activity.

62. (New) The method according to claim 1, wherein at least one of S_2-S_X is ≥ 1.

63. (New) The method according to claim 1, wherein at least one $OPGL_{c1} - OPGL_{ex}$ contains a foreign side group in the form of at least one foreign T helper lymphocyte epitope.

64. (New) The method according to claim 62, wherein at least one $OPGL_{e1} - OPGL_{ex}$ contains a foreign side group in the form of at lest one foreign T helper lymphocyte epitope.

65. (New) A method for *in vivo* down-regulation of osteoprotegerin ligand (OPGL) activity in a mammal, the method comprising effecting presentation to the mammal's immune system of an immunogenically effective amount of a modified OPGL polypeptide having general formula I:

$$(OPGL_{e1})_{n1}(MOD)_{s1}(OPGL_{s1})_{n2}....(MOD_x)_{sx}(OPGL_{ex})_{nx} \qquad (I)$$

-where $OPGL_{c1}$-$OPGL_{ex}$ are x B-cell epitope containing subsequences of OPGL which optionally contain foreign side groups in the form of at least one foreign T helper lymphocyte epitope, x is an integer ≥ 2, n1-nx are x integers ≥ 0 of which at least one is ≥ 1, MOD_1-MOD_x are x modifications in the form of at least one foreign T helper lymphocyte epitope introduced between preserved B-cell epitopes, and s_1-s_x are x integers ≥ 0 of which at least one is ≥ 1 if no optional side groups are introduced in the $OPGL_c$ sequences, whereby the mammal's own OPGL is down-regulated due to binding thereof to antibodies induced by immunization with the modified OPGL polypeptide,

OPGL being a protein which acts as an osteoclast differentiation factor and which has an amino acid sequence as set forth in SEQ ID NO: 2 for human OPGL.

66. (New) The method according to claim 65, wherein at least one of s_1-$s_x \geq 1$.

67. (New) The method according to claim 65, the modified OPGL polypeptide further comprises a modification (MODy) in the form of a foreign T helper lymphocyte epitope so as to be of the formula (II):

$$(MOD_y)(OPGL_{e1})_{n1}(MOD_1)_{s1}(OPGL_{e2})_{n2}....(MOD_x)_{sx}(OPGL_{ex})_{nx}. \qquad (II)$$

68. (New) The method according to claim 65, wherein the modified OPGL polypeptide includes a duplication of at least one OPGL B-cell epitope.

69. (New) The method according to claim 65, wherein the foreign T-cell epitope is immunodominant in the mammal.

70. (New) The method according to claim 69, wherein the foreign T-cell epitope is capable of binding to a large proportion of MHC Class II molecules.

71. (New) The method according to claim 70, wherein the at least one foreign T-cell epitope is selected from the group consisting of a natural T-cell epitope and an artificial MHC-II binding peptide sequence.

72. (New) The method according to claim 71, wherein the natural T-cell epitope is selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a *P. falciparum* CS epitope.

73. (New) The method according to claim 72, wherein the modified OPGL polypeptide contains a modification in any one of positions 171-193, any one of positions 199-219, any one of positions 222-247, any one of positions 257-262, or in any one of positions 286-317, the amino acid numbering conforming with that of SEQ ID NO: 2.

74. (New) The method according to claim 73, wherein the modification comprises a substitution of at least one amino acid sequence within a position defined in claim 73 with an amino acid sequence of equal or different length which contains a foreign T_H epitope.

75. (New) A method for treating or preventing excessive bone loss which comprises administering to a patient in need of such treatment an effective osteoproteserin ligand (OPGL)- down regulating amount of a modified OPGL polypeptide having the formula I:

$$(MOD_1)_{s1}(OPGL_{e1})_{n1}(MOD_2)_{s2}(OPGL_{e2})_{n2}....(MOD_x)_{sx}(OPGL_{ex})_{nx} \quad (I)$$

-where $OPGL_{e1}$-$OPGL_{ex}$ are x B-cell epitope containing subsequences of OPGL which independently are identical or non-identical and which optionally contain foreign side groups in the form of at least one foreign T helper lymphocyte epitope, x is an integer ≥ 3, n1-nx are x integers ≥ 0 of which at least one is ≥ 1, MOD_1-MOD_x are x modifications in the form of at least one foreign T helper lymphocyte epitope, MOD_2-MOD_x are modifications that are introduced between the preserved B-cell epitopes, and s_1-s_x are x integers ≥ 0 of which at least one is ≥ 1 if no optional side groups are introduced in the $OPGL_e$ sequences, whereby the mammal's own OPGL is down-regulated due to binding thereof to antibodies induced by immunization with the modified OPGL polypeptide,

OPGL being a protein which acts as an osteoclast differentiation factor and which has an amino acid sequence as set forth in SEQ ID NO: 2 for human OPGL.

76. (New) The method according to claim 75, wherein at least one of S_2-S_x is ≥ 1.

77. (New) The method according to claim 75, wherein the modified OPGL polypeptide includes an amino acid substitution in or deletion in or insertion in or addition to the OPGL polypeptide sequence, or any combination thereof.

78. (New) The method according to claim 75, wherein the modified OPGL polypeptide includes a duplication of at least one OPGL B-cell epitope.

79. (New) The method according to claim 75, wherein the foreign T-cell epitope is immunodominant in the mammal.

80. (New) The method according to claim 79, wherein the foreign T-cell epitope is capable of binding to a large proportion of MHC Class II molecules.

81. (New) The method according to claim 79, wherein the at least one foreign T-cell epitope is selected from the group consisting of a natural T-cell epitope and an artificial MHC-II binding peptide sequence.

82. (New) The method according to claim 81, wherein the natural T-cell epitope is selected from the group consisting of a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a *P. falciparum* CS epitope.

83. (New) The method according to any one of claims 75-82, wherein the modified OPGL polypeptide contains a modification in any one of positions 171-193, any one of positions 199-219, any one of positions 222-247, any one of positions 257-262, or in any one of positions 286-317, the amino acid numbering conforming with that of SEQ ID NO: 2.

84. (New) The method according to claim 83, wherein the modification comprises a substitution of at least one amino acid sequence within a position defined in claim 17 with an amino acid sequence of equal or different length which contains a foreign T_H epitope.

85. (New) The method according to claim 75, wherein an effective amount of the modified OPGL polypeptide is administered to the mammal via a route selected from the group consisting of parenteral route; the peritoneal route; the oral route; the buccal route; the sublinqual route; the epidural route; the spinal route; the anal route; and the intracranial route.

86. (New) The method according to claim 85, wherein the effective amount is between 0.5 μg and 2,000 μg of the modified OPGL polypeptide.

87. (New) The method according to claim 85, wherein the modified OPGL polypeptide is contained in a virtual lymph node (VLN) device.